REMARKS

Status of the Claims

Claims 1, 2 and 5-33 were previously presented for consideration, and were rejected. Claims 5, 6 and 9 were canceled. Claims 1, 8 and 32 were amended, and a new claim 56 was added. Support for amended claim 1 can be found in the specification as filed at least on page 5, lines 21-26, and in claims 5 and 6 as filed. Support for new claim 56 can be found in the specification as filed at least on page 15, lines 16-18 and page 17, lines 20-22. Thus, no new matter has been introduced by way of these amendments. Upon entry of the present amendments, claims 1, 2, 7-8, 10-33 and 56 will be pending. Reconsideration in view of the following comments is respectfully requested.

With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Rejections Under 35 U.S.C. § 112, Second Paragraph

Indefiniteness of "Eppendorf Tube"

Claim 22 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner argues that the recitation of "eppendorf tube" renders claim 22 indefinite because the Eppendorf web site lists at least 8 different types of tubes. Applicants respectfully point out that the limitation "eppendorf tube" is referred to in claim 23, not 22, and traverse this rejection.

The definiteness of a patent claim depends on whether one skilled in the art would understand the bounds of the claims when read in light of the specification. *Union Pac. Res. Co. v. Chesapeake Energy Corp.*, 236 F.3d 684, 692 (Fed. Cir. 2001) (citing *Orthokinetics, Inc. v. Safety*

Travel Chairs, Inc., 806 F.2d 1565, 1576 (Fed. Cir. 1986)). "A claim is indefinite if its legal scope is not clear enough that a person of ordinary skill in the art could determine whether a particular [product or method] infringes or not." *Geneva Pharms., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1384 (Fed. Cir. 2003).

In response to the Examiner's accurate observation that Eppendorf's web site lists several types of tubes, Applicants respectfully submit that the term "eppendorf tube" applies to any of the laboratory tubes marketed by Eppendorf. The subtle differences in the volume and shape of the tubes are immaterial to the limitation of claim 23. The standard of definiteness under 35 U.S.C. § 112, second paragraph is clear – a claim does not fail for being indefinite as long as a person of ordinary skill in the art would understand the metes and bounds of the claim. Eppendorf tubes have been a staple in laboratories around the world for over 40 years (*see* www.eppi40.com). No skilled artisan would have any difficulty understanding the meaning of "eppendorf tube." Therefore, claim 23 cannot be deemed indefinite within the meaning if 35 U.S.C. § 112, second paragraph.

Indefiniteness of "Physiological Salt Water"

Claim 32 stands rejected under 35 U.S.C. § 112, second paragraph, as being indefinite because the limitation of "physiological salt water" does not specify with clarity the composition of the solution in question. In response, Applicants have amended claim 32 to delete the reference to "physiological salt water."

For the reasons stated above, Applicants respectfully request that the two rejections under 35 U.S.C. § 112, second paragraph be withdrawn and claims 23 and 32 be allowed in their present form.

Rejection Under 35 U.S.C. § 102(b)

Claims 1-2, 5-9, 11, 13-15, 22, 24-33 were rejected under 35 U.S.C. § 102(b) as being anticipated by Antoine, et al. (*Immunochemistry*, 1978, 15(7): 443-452). The Examiner based his conclusion on the fact that Antoine, et al. teaches a method using iron oxide embedded

polyacrylamide-agarose microbeads coated with anti-mouse or anti-rat Ig to isolate mouse or rat lymphoid cells from blood or plasma, magnetically separating the conjugate, washing the cells with PBS buffer (pH 7.4 or about pH 6.5), and eluting the cells from the microbeads then removing the microbeads. For the reasons stated below, Applicants respectfully traverse this rejection.

The legal standard for anticipation under 35 U.S.C. § 102 is one of strict identity. *Trintec Industries, Inc. v. Top-U.S.A. Corp.*, 63 U.S.P.Q.2d 1597 (Fed. Cir. 2002). To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. *In re Paulson*, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994) (citing *In re Spada*, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987); MPEP §2131.

Claim 1 of the present invention and all the claims depending therefrom contain one important limitation: a magnetic microbead not comprising a moiety that binds to a target cell, cellular organelle or virus with high specificity. Furthermore, the specification expressly explains that "the binding between the magnetic microbead and the target cell, cellular organelle or virus is not mediated by a specific interaction between ligand and receptor, antigen and antibody..." (see page 5, lines 16-18; emphasis added). The specification further clarifies that the magnetic microbeads contemplated by the present invention do not comprise "a biomolecule such as an amino acid, a peptide, a protein... [or] an antibody that specifically binds to the target cell, cellular organelle or virus" (see page 5, lines 22-26; emphasis added).

Antoine, et al. teaches a "method of fractionation of mouse and rat lymphoid cells using as an insoluble support polyacrylamide-agarose spherical beads in which iron oxide particles were trapped (Magnogel) and coated with purified anti-mouse or anti-rat Ig antibodies" (see abstract; emphasis added). Furthermore, Antoine, et al. teaches that "99.6 – 99.9% of the cells not retained on anti-Ig coated Magnogel were devoid of surface immunoglobulins" (see id.). Based on the foregoing, it becomes abundantly clear that the method of fractionation taught by Antoine, et al.,

much like many other prior art references, is based on specific binding between antigen and antibody. Thus, Antoine, et al. does not contain the limitation of having a magnetic microbead not comprising a moiety that binds to a target cell, cellular organelle or virus with high specificity, as required by claim 1 of the present invention.

Since Antoine, et al. does not teach each and every element of claim 1 and claims depending therefrom, the strict identity standard of anticipation under 35 U.S.C. § 102 is not met. Accordingly, Applicants respectfully request that this rejection 35 U.S.C. § 102(b) be withdrawn and claims 1-2, 7-8, 11, 13-15, 22, 24-33 allowed.

Rejections Under 35 U.S.C. § 103(a)

Obviousness over Antoine, et al. in View of Ullman, et al.

Claims 10, 12, 16, 17, and 22 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Antoine, et al. in view of Ullman, et al. (U.S. Pat. No. 5,536,644). The Examiner asserts that Ullman, et al. teaches use of a microbead sized between 2×10^{-8} and 1×10^{-4} m (column 6, lines 65 forward), polymeric microbeads comprising hydroxyl groups (column 7, lines 32 (alcohol) and 34 (free hydroxyl)), a clinical specimen (column 16, lines 62-64), a sample comprising blood (column 13, lines 39-41), and the time of completing the method of 15-85 sec (column 18 lines 18-31, especially line 27). The Examiner further argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Antoine, et al. by using the limitations described above as taught by Ullman, et al. Applicants respectfully traverse this rejection.

The Examiner bears the burden of establishing a *prima facie* case of obviousness. *In re Rijckaert*, 9 F.3d 1531, 1532 (Fed. Cir. 1993). Only if this burden is met does the burden of coming forward with rebuttal argument or evidence shift to the applicant. *Id.* at 1532. When the references cited by the examiner fail to establish a *prima facie* case of obviousness, the rejection is improper and will be overturned. *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988). A *prima facie* case of obviousness requires the satisfaction of three requirements. First, the combined prior art references

must teach or suggest all of the claim limitations. *In re Royka*, 490 F.2d 981, 985 (CCPA 1974); MPEP § 2143.03. Second, there must be some teaching, suggestion or motivation, found either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference to achieve the claimed invention. *In re Kahn*, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006); MPEP § 2143.01. And third, there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991); MPEP § 2143.02.

I. The Cited References Do Not Teach or Suggest All of the Claim Limitations

"To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." MPEP § 2143.03 citing *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). As discussed earlier, Antoine, et al. does not teach using a magnetic microbead not comprising a moiety that binds to a target cell, cellular organelle or virus with high specificity. The addition of Ullman, et al. does not correct that fatal deficiency. Furthermore, most of the specific teachings of Ullman, et al. referred to by the Examiner relate to non-magnetic particles, not to magnetic microbeads as claimed in the present invention (*see* Ullman, column 6, line 63; column 7, line 25; column 13, lines 38-39, etc.). Accordingly, the combination of Antoine, et al. and Ullman, et al. does not teach all of the limitations of claims 10, 12, 16, 17, and 22, which means that the Examiner has failed to establish *prima facie* obviousness under 35 U.S.C. § 103(a).

II. There is No Motivation to Combine or Modify the Cited References to Achieve the Claimed Invention

To establish a *prima facie* case of obviousness, the Examiner must demonstrate some teaching, suggestion or motivation, found either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference to achieve the claimed invention. MPEP § 2143.01 citing *In re Kahn*, 441 F.3d 977, 986, 78 USPQ2d 1329, 1335 (Fed. Cir. 2006). "There are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art." MPEP § 2143.01 quoting *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). Although the U.S. Supreme Court in *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727

(2007) rejected a rigid application of the "teaching, suggestion, or motivation" ("TSM") test, it did not totally reject the use of "teaching, suggestion, or motivation" as a factor in the obviousness analysis (*see* Margaret A. Focarino, *Memorandum to Technology Center Directors Re: Supreme Court Decision on* KSR Int'l Co. v. Teleflex, Inc., May 3, 2007). The Court noted that the analysis supporting a rejection under 35 U.S.C. § 103(a) "should be made explicit," and that it was still "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does." *See KSR* at 1741.

In this case, it is not clear where such teaching, suggestion or motivation would come from. Evidently, Antoine, et al. teaches a rather efficient method of specific cell fractionation, whereby up to 400-fold depletion of immunoglobulin-positive cells may be achieved. The method claimed in the present invention, on the other hand, accomplishes non-specific separation of target cells, cellular organelles or viruses from a given sample containing or suspected of containing such cells, organelles or viruses. Since the problems to be solved are radically different, a person of ordinary skill in the art would not have been motivated to modify the teachings of Antoine, et al. to achieve the claimed invention. Accordingly, the Examiner has failed to establish *prima facie* obviousness.

III. A Skilled Artisan Would Not Have a Reasonable Expectation of Success in Achieving the Claimed Invention Based on the Combined Teachings of the Cited References

Obviousness does not require absolute predictability, however, at least some degree of predictability is required. MPEP § 2143.02 citing *In re Rinehart*, 531 F.2d 1048, 189 USPQ 143 (Fed. Cir. 1976). Applicants respectfully submit that one of ordinary skill in the art would not have had a reasonable expectation of success in practicing the claimed invention based on the teachings of Antoine, et al. in view of Ullman, et al.

As explained above, Antoine, et al. teaches a method of specific, antibody-based cell fractionation. Ullman, et al. teaches a method of cell separation using Ferrofluid, namely magnetic particles coated with proteins such as succinylated bovine serum albumin or rabbit serum albumin (*see* Example 4). In contrast, the present invention claims a method of rapid cell separation wherein the magnetic beads are not coated with any proteins, antibodies or other moieties that bind to target

cells, cellular organelles or viruses with high specificity (*see* amended claim 1). Thus, the combined teachings of Antoine, et al. and Ullman, et al. do not provide the threshold level of predictability of success in achieving the claimed invention that is required in order to establish *prima facie* obviousness under 35 U.S.C. § 103(a).

Obviousness over Antoine, et al. in View of Brinchmann, et al.

Claims 18-21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Antoine, et al. in view of Brinchmann, et al. (*Journal of Virology*, 1991, 65(4): 2019-2023). The Examiner asserts that Brinchmann, et al. teaches a method of separating HIV-infected cells from whole blood, washing the cell, isolating either HIV RNA or HIV DNA and amplifying the oligonucleotides (PCR of *pol* gene). The Examiner further invokes MPEP § 2144.04 quoting *In re Venner* for the proposition that "broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art." Accordingly, the Examiner argues that it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Antoine, et al. by using the limitation of the claims as taught by Brinchmann, et al. Applicants respectfully disagree and therefore traverse this rejection.

I. The Cited References Do Not Teach or Suggest All of the Claim Limitations

As discussed above, Antoine, et al. teaches a method of specific, Ig antibody-based cell fractionation. Similarly, Brinchmann, et al. teaches a method of isolating $CD4^+$ T cells using Dynabeads coated with an anti-CD4 monoclonal antibody (*see* pages 2019-2020). Thus, neither reference teaches a method of using magnetic microbeads not comprising a moiety that binds to a target cell, cellular organelle or virus with high specificity. Accordingly, the combination of Antoine, et al. and Brinchmann, et al. does not teach all of the limitations of claims 18-21, which means that the Examiner has failed to establish *prima facie* obviousness under 35 U.S.C. § 103(a).

II. There is No Motivation to Combine or Modify the Cited References to Achieve the Claimed Invention

Just as in the preceding discussion of Antoine in view of Ulmann, Applicants fail to see any teaching, suggestion or motivation to modify or combine the references. Once again, Antoine, et al. teaches a method of specific cell fractionation, whereby efficient depletion of Ig-positive cells may be accomplished. Similarly, Brinchmann, et al. teaches a method of specific cell isolation using a monoclonal anti-CD4 antibody. The method claimed in the present invention, on the other hand, accomplishes non-specific separation of target cells, cellular organelles or viruses from a given sample containing or suspected of containing such cells, organelles or viruses. Since the problems to be solved are so different, a skilled artisan would not have been motivated to modify the teachings of Antoine, et al. or Brinchmann, et al. to achieve the claimed invention. Therefore, the Examiner has failed to establish the motivation prong of *prima facie* obviousness.

III. A Skilled Artisan Would Not Have a Reasonable Expectation of Success in Achieving the Claimed Invention Based on the Combined Teachings of the Cited References

Applicants respectfully submit that one of ordinary skill in the art would not have had a reasonable expectation of success in practicing the claimed invention based on the teachings of Antoine, et al. in view of Brinchmann, et al.

As explained above, Antoine, et al. teaches a method of specific, antibody-based cell fractionation. Similarly, Brinchmann, et al. teaches a method of isolating CD4-positive T cells using a monoclonal anti-CD4 antibody. In contrast, the present application claims a method of rapid cell separation wherein the magnetic beads are not coated with any proteins, antibodies or other moieties that bind to target cells, cellular organelles or viruses with high specificity (*see* amended claim 1). Thus, the combined teachings of Antoine, et al. and Brinchmann, et al. do not provide the threshold level of predictability of success in achieving the claimed invention that is required in order to establish *prima facie* obviousness under 35 U.S.C. § 103(a).

The fact that Brinchmann, et al. teaches a method of separating HIV-infected cells from whole blood, washing the cell, isolating either HIV RNA or HIV DNA and amplifying the

oligonucleotides using PCR automation is irrelevant to the present discussion because neither Brinchmann nor Antoine teaches protein-free magnetic separation claimed in the present invention. Furthermore, the discussion of *In re Venner* is not appropriate here because the method claimed in the present invention is easily distinguishable over the prior art regardless of whether it is practiced manually or automatically. Clearly, Applicants are not merely trying to claim an automatic or mechanical substitute to unpatentable manual activity which accomplishes the same result.

Conclusion

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 514572000600.

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Respectfully submitted,

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